HUBR 10673 DIV (10185485)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Applicant	:	Christophe Seidel, et al.
Serial No.	:	09/896,032
Filed	:	June 29, 2001
For	:	METHOD FOR DETERMINING EARLY HCV SEROCONVERSION
Art Unit	:	1648
Examiner	:	Donna C. Wortman

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION

Dr. Ursula-Henrike Wienhues-Thelen hereby states as follows:

1. I am one of the coinventors of the invention described in the above referenced patent application. At the time the original application in the series of applications leading to the present application was filed, I was known as Ursula-Henrike Wienhues. "Wienhues-Thelen" is my married name.

2. I am familiar with the prosecution of the above referenced application, and the applications filed and prosecuted before it.

3. I have considered the English language translation of JP06074956 provided by the Examiner, and I would like to comment on why it is irrelevant to the invention claimed in this application. For simplicity, I will refer to this document as "JP '956".

4. The JP '956 application discusses how HCV antibodies can be determined, in diluted sera when using a reducing buffer, using the NS3 antigen.

5. This is decidedly NOT the same thing as determining early seroconversion in a sample. The reasons for this are multifold.

6. First of all, antibodies that are present in an early seroconversion sample differ significantly from those antibodies that are present in a high titer sample taken from a chronically ill patient, which was the sample type used in JP '956 before dilution sensitivity determination were carried out. For example, seroconversion antibodies differ from antibodies present at an advanced stage of infection, in that they show lower affinity, because they are mainly of IgM class, and have different specificity.

7. In addition, seroconversion antibodies differ from others in their specificity against viral epitopes. The impact of reducing buffer conditions on the presentation of epitopes of NS3 recognized by early seroconversion antibodies, and the effect of reducing buffer conditions on the binding affinity of epitopes to early seroconversion antibodies are not suggested by JP '956.

8. There is scientific evidence of this. For example, see WO 99/15901 (Chiron), Ziegler, et al., Poster Presentation, Berlin 1999; WO 99/54735 (Innogenetics), Wolter, et al., *Clin. Lab*, 43:125-135 (1997); Hino, *Intervirology*, 37:77-86 (1994); Barrera, et al., *Vox Sang*, 68:15-18 (1995); and Heyermann, et al., *Clin. Lab*, 44:903-905 (1998). Copies of these will be provided upon request.

9. The additional references that are used by the Examiner do not change these failings. Beach et al. discusses the temporal relationships of HCV RNA and antibody responses when chimpanzees were inoculated, but does not deal with human studies. No conclusions can be reached on the determination of HCV seroconversion in humans. Beach et al. profess this, at page 234, second paragraph of Discussions, lines 7-9.

10. The Vallari reference discusses serological markers of posttransfusion hepatis C viral infection. At page 555, the second paragraph of the Discussion, line 11, the core antigen, not the NS3 antigen, was cited as the antigen to which response was

most frequent. Nothing at all suggests that one could use reducing buffers, in assays for NS3 antigens, to determine early seroconversion.

11. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information or belief are believed to be true; and further that these statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements and the like so made may jeopardize the validity of this declaration, the subject application, or any patent issued thereon.

13.01.2004 Ursula-Henrike Weinhues-Thelen

Date Ursula-Henrike Weinhues-Thelen